

Appendix 4: Comparison of univariable associations with mortality and morbidity before discharge, between English 1995 and 2006 cohorts, gestational age between 22 and 25 weeks [posted as supplied by author]

In each table statistical significance is indicated: * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$. # = marginally significant result ($0.05 < p \leq 0.1$)

In 2006 only 13 of 1116 admitted babies did not receive surfactant therapy.

i) Population: Babies admitted for intensive care. Outcome death before discharge

Variable, yes/no unless stated	1995 n=666 admissions, 400 deaths	2006 n=1115 admissions, 523 deaths	Ratio of odds ratios 2006/1995 ¹
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Gestational age per decimal week	0.47 (0.38 to 0.58)***	0.42 (0.36 to 0.50)***	0.90 (0.69 to 1.18)
Birthweight per 100g	0.60 (0.52 to 0.69)***	0.61 (0.55 to 0.68)***	1.03 (0.86 to 1.22)
Birthweight SD	0.71 (0.58 to 0.86)***	0.76 (0.64 to 0.89)***	1.07 (0.83 to 1.38)
Multiple birth	1.35 (0.95 to 1.91)#	1.60 (1.22 to 2.09)***	1.18 (0.76 to 1.84)
Male	1.34 (0.98 to 1.83)#	1.38 (1.09 to 1.75)***	1.05 (0.71 to 1.55)
Obstetric problems:			
Pre-eclampsia	1.70 (0.65 to 4.43)	0.98 (0.56 to 1.71)	0.58 (0.19 to 1.75)
PROM >24h	0.74 (0.52 to 1.06)#	0.81 (0.62 to 1.05)	1.09 (0.70 to 1.70)
Cervical suture	0.57 (0.34 to 0.98)*	0.73 (0.46 to 1.16)	1.27 (0.63 to 2.58)
APH	1.24 (0.87 to 1.77)	0.81 (0.60 to 1.09)	0.66 (0.42 to 1.06)#
Chorioamnionitis	0.47 (0.31 to 0.69)***	0.69 (0.52 to 0.93)*	1.49 (0.91 to 2.43)
Any ante-natal steroid	0.41 (0.29 to 0.58)***	0.43 (0.31 to 0.59)***	1.04 (0.65 to 1.69)
Antenatal steroid >24h before birth	0.53 (0.39 to 0.73)***	0.53 (0.42 to 0.67)***	1.00 (0.67 to 1.49)
Tocolysis	0.60 (0.43 to 0.86)**	0.65 (0.5 to 0.84)***	1.07 (0.70 to 1.66)
Maternal age per additional 10 yr	0.82 (0.63 to 1.07)	0.82 (0.68 to 0.98)*	1.00 (1.00 to 1.00)
Ethnicity = black	0.72 (0.47 to 1.10)	0.72 (0.53 to 0.97)*	0.99 (0.59 to 1.67)
Vaginal delivery	0.89 (0.59 to 1.34)	1.26 (0.94 to 1.70)	1.43 (0.86 to 2.38)
Heart rate >100bpm at 5 minutes	0.30 (0.17 to 0.52)***	0.39 (0.25 to 0.60)***	1.29 (0.64 to 2.62)
Admission temperature >35°C	0.29 (0.20 to 0.41)***	0.49 (0.36 to 0.68)***	1.69 (1.05 to 2.73)*
CRIB-I score per point	1.37 (1.30 to 1.45)***	1.26 (1.21 to 1.30)***	0.92 (0.86 to 0.98)**
Transferred within 24h of birth	1.43 (0.92 to 2.22)	0.97 (0.72 to 1.30)	0.68 (0.40 to 1.16)
Any surfactant treatment	1.00 (0.63 to 1.57)	N/A	N/A

1. This is the odds ratio of the interaction of cohort and predictor variable after adjustment for the predictor and cohort variables. Statistical significance implies that the association with the predictor is different in the two cohorts.

PROM = Prolonged Rupture of Membranes >24 hours before birth

APH = Ante-partum haemorrhage

- ii) Population: survivors to discharge. Outcome severe cerebral ultrasound scan abnormality (ventriculomegaly, echodense haemorrhagic parenchymal infarct and/or parenchymal cysts) on last available cerebral ultrasound scan.

Variable, yes/no unless stated	1995 n=266 survivors, 41 with severe scan abnormality	2006 n=590 survivors, 82 with severe scan abnormality	Ratio of odds ratios 2006/1995 ¹
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Gestational age per decimal week	0.84 (0.53 to 1.33)	1.28 (0.92 to 1.78)	1.53 (0.86 to 2.7)
Birthweight per 100 gram	1.21 (0.89 to 1.65)	1.00 (0.83 to 1.22)	0.83 (0.58 to 1.19)
Birthweight SD	1.5 (0.97 to 2.33)#	0.78 (0.57 to 1.07)	0.52 (0.30 to 0.89)*
Multiple birth	0.95 (0.44 to 2.06)	0.99 (0.57 to 1.75)	1.05 (0.4 to 2.72)
Male	1.10 (0.56 to 2.14)	1.45 (0.91 to 2.32)	1.35 (0.60 to 3.03)
Obstetric problems:			
Pre-eclampsia	1.09 (0.12 to 9.58)	1.77 (0.69 to 4.50)	1.62 (0.15 to 17.27)
PROM >24 hours	0.49 (0.21 to 1.16)	0.82 (0.48 to 1.40)	1.67 (0.61 to 4.61)
Cervical suture	1.05 (0.38 to 2.92)	0.40 (0.12 to 1.30)	0.38 (0.08 to 1.81)
APH	1.18 (0.55 to 2.51)	1.08 (0.62 to 1.91)	0.92 (0.36 to 2.37)
Chorioamnionitis	0.45 (0.18 to 1.11)#	0.63 (0.35 to 1.15)	1.43 (0.48 to 4.25)
Any ante-natal steroid	1.13 (0.49 to 2.59)	0.86 (0.43 to 1.72)	0.76 (0.26 to 2.26)
Antenatal steroid >24 hours before birth	0.45 (0.22 to 0.9)*	0.55 (0.34 to 0.88)*	1.22 (0.53 to 2.84)
Tocolysis	1.65 (0.83 to 3.29)	0.63 (0.37 to 1.05)#	0.38 (0.16 to 0.89)*
Maternal age per additional 10 years	1.13 (0.64 to 1.99)	0.74 (0.51 to 1.08)	1.00 (0.99 to 1.00)
Ethnicity = black	0.44 (0.15 to 1.31)	0.51 (0.26 to 1.00)*	1.15 (0.32 to 4.11)
Vaginal delivery	2.00 (0.67 to 5.93)	0.72 (0.42 to 1.23)	0.36 (0.11 to 1.21)
Heart rate >100 beats per minute at 5 minutes	0.86 (0.23 to 3.12)	1.62 (0.48 to 5.44)	1.89 (0.32 to 11.13)
Admission temperature >35°C	0.83 (0.39 to 1.78)	1.03 (0.50 to 2.09)	1.24 (0.44 to 3.51)
CRIB-I score per point	1.05 (0.96 to 1.16)	1.02 (0.96 to 1.09)	0.97 (0.87 to 1.09)
Transferred within 24 hours of birth	3.82 (1.71 to 8.53)***	1.42 (0.83 to 2.45)	0.37 (0.14 to 0.98)*
Any surfactant treatment	1.53 (0.51 to 4.60)	N/A	N/A

1. This is the odds ratio of the interaction of cohort and predictor variable after adjustment for the predictor variable. Statistical significance implies that the association with the predictor is different in the two cohorts.

PROM = Prolonged rupture of membranes >24 hours before birth.

APH= Ante-partum haemorrhage

- iii) Population: survivors to discharge. Outcome: bronchopulmonary dysplasia (continued oxygen supplementation at 36 weeks post-menstrual age).

Variable, yes/no unless stated	1995 n=266 survivors, 199 in oxygen at 36w pma	2006 n=593 survivors, 433 in oxygen at 36w pma	Ratio of odds ratios 2006/1995 ¹
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Gestational age per decimal week	0.61 (0.39 to 0.94)*	0.52 (0.39 to 0.69)***	0.85 (0.51 to 1.43)
Birthweight per 100 gram	0.79 (0.61 to 1.02)#	0.62 (0.53 to 0.73)***	0.78 (0.58 to 1.06)
Birthweight SD	0.85 (0.59 to 1.22)	0.53 (0.41 to 0.70)***	0.63 (0.40 to 0.99)*
Multiple birth	1.10 (0.58 to 2.09)	1.32 (0.84 to 2.08)	1.20 (0.54 to 2.64)
Male	1.76 (1.00 to 3.1)*	2.03 (1.39 to 2.95)***	1.12 (0.57 to 2.20)
Obstetric problems:			
Pre-eclampsia	0.65 (0.12 to 3.61)	1.12 (0.47 to 2.68)	1.73 (0.25 to 11.92)
PROM >24 hours	0.82 (0.44 to 1.51)	0.97 (0.65 to 1.44)	1.19 (0.57 to 2.47)
Cervical suture	0.55 (0.25 to 1.22)	1.99 (0.91 to 4.35)#	3.63 (1.19 to 11.08)*
APH	1.09 (0.56 to 2.11)	1.08 (0.69 to 1.7)	0.99 (0.45 to 2.21)
Chorioamnionitis	0.79 (0.42 to 1.48)	0.87 (0.57 to 1.32)	1.10 (0.52 to 2.32)
Any ante-natal steroid	1.42 (0.74 to 2.74)	1.33 (0.78 to 2.27)	0.93 (0.40 to 2.17)
Antenatal steroid >24 hours before birth	1.03 (0.59 to 1.80)	0.90 (0.62 to 1.30)	0.87 (0.45 to 1.71)
Tocolysis	1.28 (0.69 to 2.35)	1.22 (0.83 to 1.78)	0.95 (0.47 to 1.96)
Maternal age per additional 10 years	0.88 (0.55 to 1.40)	1.12 (0.84 to 1.49)	1.00 (1.00 to 1.01)
Ethnicity = black	0.89 (0.44 to 1.80)	0.94 (0.61 to 1.46)	1.06 (0.46 to 2.44)
Vaginal delivery	1.69 (0.84 to 3.39)	1.02 (0.66 to 1.59)	0.61 (0.27 to 1.38)
Heart rate >100 beats per minute at 5 minutes	0.89 (0.28 to 2.83)	1.38 (0.65 to 2.91)	1.55 (0.39 to 6.14)
Admission temperature >35°C	0.44 (0.20 to 0.95)*	0.40 (0.20 to 0.79)**	0.91 (0.32 to 2.57)
CRIB-I score per point	1.14 (1.05 to 1.25)**	1.16 (1.10 to 1.23)***	1.01 (0.91 to 1.13)
Transferred within 24 hours of birth	2.80 (0.95 to 8.25)#	0.76 (0.49 to 1.18)	0.27 (0.08 to 0.87)*
Any surfactant treatment	3.69 (1.70 to 7.63)***	N/A	N/A

1. This is the odds ratio of the interaction of cohort and predictor variable after adjustment for the predictor variable. Statistical significance implies that the association with the predictor is different in the two cohorts.

PROM = Prolonged Rupture of Membranes >24 hours before birth

APH = Ante-partum haemorrhage

iv: Population: survivors to discharge. Outcome: continued oxygen supplementation at 40 weeks post-menstrual age.

Variable, yes/no unless stated	1995 n=266 survivors, 140 in oxygen at 40w pma	2006 n=592 survivors, 314 in oxygen at 40w pma	Ratio of odds ratios 2006/1995 ¹
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Gestational age per decimal week	0.49 (0.34 to 0.71)***	0.58 (0.46 to 0.73)***	1.18 (0.76 to 1.83)
Birthweight per 100 gram	0.76 (0.60 to 0.95)*	0.65 (0.56 to 0.75)***	0.86 (0.66 to 1.12)
Birthweight SD	0.91 (0.66 to 1.25)	0.60 (0.47 to 0.75)***	0.65 (0.44 to 0.97)*
Multiple birth	1.35 (0.77 to 2.36)	1.40 (0.95 to 2.08)#	1.04 (0.52 to 2.06)
Male	1.84 (1.13 to 3.00)*	1.54 (1.11 to 2.13)**	0.88 (0.49 to 1.58)
Obstetric problems:			
Pre-eclampsia	0.43 (0.08 to 2.42)	1.19 (0.55 to 2.57)	2.75 (0.42 to 17.97)
PROM >24 hours	1.02 (0.60 to 1.75)	1.08 (0.76 to 1.54)	1.06 (0.55 to 2.01)
Cervical suture	0.94 (0.44 to 1.98)	1.10 (0.61 to 1.98)	1.17 (0.45 to 3.04)
APH	1.09 (0.62 to 1.92)	0.93 (0.63 to 1.39)	0.86 (0.43 to 1.71)
Chorioamnionitis	0.78 (0.45 to 1.36)	0.85 (0.59 to 1.24)	1.09 (0.56 to 2.11)
Any ante-natal steroid	1.15 (0.64 to 2.08)	0.92 (0.56 to 1.52)	0.80 (0.37 to 1.73)
Antenatal steroid >24 hours before birth	1.21 (0.75 to 1.97)	1.05 (0.75 to 1.45)	0.86 (0.48 to 1.54)
Tocolysis	1.41 (0.84 to 2.38)	1.35 (0.96 to 1.88)#	0.95 (0.51 to 1.78)
Maternal age per additional 10 years	0.85 (0.57 to 1.28)	0.92 (0.71 to 1.18)	1.00 (1.00 to 1.01)
Ethnicity = black	0.79 (0.42 to 1.48)	1.18 (0.80 to 1.75)	1.49 (0.71 to 3.11)
Vaginal delivery	1.27 (0.66 to 2.42)	1.00 (0.67 to 1.47)	0.79 (0.37 to 1.68)
Heart rate >100 beats per minute at 5 minutes	0.99 (0.37 to 2.65)	0.83 (0.41 to 1.68)	0.83 (0.25 to 2.81)
Admission temperature >35°C	0.40 (0.22 to 0.75)**	0.58 (0.35 to 0.97)*	1.44 (0.65 to 3.20)
CRIB-I score per point	1.17 (1.08 to 1.26)***	1.13 (1.08 to 1.19)***	0.97 (0.89 to 1.06)
Transferred within 24 hours of birth	2.40 (1.10 to 5.24)*	0.84 (0.56 to 1.25)	0.35 (0.15 to 0.84)*
Any surfactant treatment	2.51 (1.20 to 5.26)*	N/A	N/A

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PROM = Prolonged Rupture of Membranes >24 hours before birth

APH = Ante-partum haemorrhage

v) Population: survivors to discharge. Outcome: Treated Retinopathy of Prematurity

Variable, yes/no unless stated	1995 n=262 survivors, 35 treated for ROP	2006 n=593 survivors, 127 treated for ROP	Ratio of odds ratios 2006/1995 ¹
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Gestational age per decimal week	0.56 (0.34 to 0.90)*	0.53 (0.41 to 0.69)***	0.96 (0.55 to 1.66)
Birthweight per 100 gram	0.74 (0.53 to 1.03)#	0.60 (0.50 to 0.72)***	0.81 (0.55 to 1.18)
Birthweight SD	1.03 (0.64 to 1.66)	0.68 (0.51 to 0.89)**	0.66 (0.38 to 1.14)
Multiple birth	0.71 (0.30 to 1.72)	1.89 (1.22 to 2.94)**	2.66 (1.00 to 7.11)#
Male	0.65 (0.31 to 1.34)	1.12 (0.75 to 1.65)	1.77 (0.78 to 4.00)
Obstetric problems:			
Pre-eclampsia	0 (0.0 to 4.12)	0.80 (0.30 to 2.14)	Not defined
PROM >24 hours	1.29 (0.60 to 2.79)	0.94 (0.61 to 1.45)	0.73 (0.30 to 1.77)
Cervical suture	1.73 (0.65 to 4.60)	1.08 (0.53 to 2.17)	0.62 (0.19 to 2.07)
APH	2.69 (1.28 to 5.65)**	0.81 (0.49 to 1.33)	0.30 (0.12 to 0.73)**
Chorioamnionitis	1.15 (0.52 to 2.54)	0.83 (0.52 to 1.32)	0.72 (0.29 to 1.81)
Any ante-natal steroid	0.64 (0.29 to 1.42)	0.61 (0.35 to 1.05)#	0.95 (0.36 to 2.52)
Antenatal steroid >24 hours before birth	1.04 (0.51 to 2.12)	0.78 (0.52 to 1.15)	0.75 (0.33 to 1.69)
Tocolysis	0.97 (0.45 to 2.09)	0.82 (0.54 to 1.24)	0.85 (0.36 to 2.03)
Maternal age per additional 10 years	1.68 (0.91 to 3.13)#	1.00 (0.74 to 1.37)	0.99 (0.99 to 1.00)
Ethnicity = black	0.12 (0.02 to 0.87)*	0.41 (0.23 to 0.74)**	3.57 (0.44 to 29.07)
Vaginal delivery	1.56 (0.52 to 4.67)	1.41 (0.85 to 2.34)	0.90 (0.27 to 3.02)
Heart rate >100 beats per minute at 5 minutes	1.15 (0.25 to 5.26)	1.01 (0.43 to 2.38)	0.88 (0.15 to 5.04)
Admission temperature >35°C	0.67 (0.30 to 1.50)	0.75 (0.43 to 1.33)	1.13 (0.42 to 3.04)
CRIB-I score per point	1.05 (0.95 to 1.16)	1.18 (1.11 to 1.24)***	1.12 (1.00 to 1.26)#
Transferred within 24 hours of birth	1.85 (0.74 to 4.65)	1.07 (0.66 to 1.73)	0.58 (0.20 to 1.63)
Any surfactant treatment	0.56 (0.22 to 1.41)	N/A	N/A

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APH = Ante-partum haemorrhage